Author's response to reviews

Title: New Side-view Imaging Technique for Observing Posterior Chamber Structures During Cataract Surgery in Porcine Eyes

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Version: 2 Date: 27 February 2013

Author's response to reviews: see over
Re: Ms: 1247029243856411
“Side-View Cinematography for Observing Posterior Chamber Structures in a Closed Eye Cataract Surgery Porcine Model”

February 27, 2013

To the Editor:

We are re-submitting our revised manuscript (MS 1247029243856411) to be re-considered for publication in BMC Ophthalmology. We thank you for allowing us to re-submit this paper. Modifications have been made on a point-by-point way in response to the reviewers’ comments, and they are underlined in the manuscript. The changes are described in more detail below.

Reviewer 1: Comments by reviewer Dr. Ryan M. Perdig

SUMMARY AND MAJOR COMPULSORY REVISIONS

The authors present a model for viewing how cataract surgery may damage the posterior chamber structures (PCS) of the eye. While such models are important, it is unclear how much more understanding is gleaned from this model versus those already reported. The authors state (or, at least, imply) that their model offers two improvements: a “3-D view” of the PCS and a “closed-eye” approach. The 3-D view is presented in the work by Assia and Apple (1992) and, while the authors cite this study, they never explain why their visualization approach is an improvement to it (this comparison should be given).

The second feature of the model, the closed-eye technique, appears to offer the opportunity to retain the IOP spikes that may be imposed during normal cataract surgery – this could be important and it is worth evaluating. However, the authors do not fully explore this point: there is no rigorous assessment of whether increased IOP during surgery actually has an adverse effect on the PCS or at what IOP damage would be expected to occur. Further, while zonular stresses are often mentioned, no quantification is given. Such evaluation would provide more motivation for using this model, thus dramatically improving the study.

RESPONSE: We have described a new method of improving the quality of viewing the posterior chamber structures (PCSs) during cataract surgery in a closed-eye system. The fundamental difference of our model with the earlier models is that cataract surgery could be performed under conditions that mimicked that of human cataract surgery. Our model allowed us to watch and record the surgery through an operating microscope (surgeon’s view) and also the movement and tension on the
PSCs on a monitor screen. Because this was a closed-eye system, we were able to measure the intraocular pressure during all procedures of the surgery. Therefore, all of the observed movements of the PCSs most likely occur during human cataract surgery. The irrigating solution we used contained fluorescent beads which allowed us to view the flow of the irrigation solution. A detailed quantitative analysis of the relationship of PCSs damage and intraocular pressure is our next step but this is beyond the scope of this report. However in the revised manuscript, we have cited our previous publication (Arch Ophthalmol. 2011, 129:751-757) in which a more detailed description of the changes in the PCSs and IOPs were reported (Lines 267-269).

Additional point 1

The authors state that their model offers a “3-D view” of the PCS, but they image these structures with one camera at a single orientation. This approach would only provide a 2-D view because the structures are viewed from a single imaging plane. A 3-D view requires imaging the same structures with at least two camera orientations. The authors need to explain what they mean by 3-D versus 2-D views.

RESPONSE. Our side-viewing technique can provide more information than the Miyake-Apple view because we can observe the PCSs. Details of the movements of the equatorial region of the zonular fibers and movements of the PCSs can be monitored easily using this method. To avoid confusion and for clarity, we have revised the manuscript by removing the word 3-D.

Additional point 2

(Lines 228 – 230). The zonular fibers are a quite dense network around the lens equator, so this reviewer is not convinced that the trapping of fluorescein beads by this tissue indicates anything about the stresses of the fibers. Again, stress is a quantity that must be rigorously computed. Further, whatever stresses may exist could be more due to the accommodative state of the eye versus those imposed by surgery. Rewording or exclusion of this point is recommended.

RESPONSE. We have reported (Arch Ophthalmol 2011;129: 751-7) that by using 1.0-µm fluorescein beads, we were able to demonstrate that the posterior chamber-anterior hyaloid membrane can act as a barrier to particulate materials including bacteria. In that paper, observations through the Miyake-Apple view of the fluorescein beads trapped in the zonule fibers allowed us to identify 5 different staining patterns: AC, Zinn, AHM, AHT, and rupture types, listed from the type with the
lowest pressure to that with the highest pressure. We have added this information in the revised manuscript (Lines 267-269).

Additional point 3  
(Lines 280 – 282). Similar to point 2, it is unclear how the trapping of beads in the zonules indicates a high zonular tension. The authors could provide empirical data quantifying the degree of bead accumulation as a function of IOP. Also, the authors should indicate the size of the beads and how this compares to the size of bacteria to further support the idea that the zonules act as a filter, which seems to be a bit far-reaching.

RESPONSE. The diameter of the fluorescein beads is 1.0-µm which is similar to that of bacteria that can cause postoperative endophthalmitis. We suggest that the trapping of beads in the zonular fibers indicates that this barrier may prevent bacteria from passing into the vitreous. As mentioned, evaluations of the IOP and the barrier function of the zonular fibers are beyond the scope of this study. However, our findings suggest that using this side-view model will make it possible to perform future studies exploring the relationship between the IOP changes and morphological and functional changes of the zonular fibers.

We have added information of the bead size (Lines 211-213) and more discussion in the revised paper (Lines 264-267).

MINOR COMPULSORY REVISIONS

Additional point 4  
(Lines 219 – 221 of the original version). The authors state that “It is noteworthy that imaging of the stress to the zonular fibers during…”. Stress is a mathematical quantity that must be computed, so it cannot be “imaged”. Perhaps the authors mean “deformation”. Rewording is suggested.

RESPONSE. Rewording and clarification have been made in the revised manuscript (Lines 208-209).

Additional point 5  
(Lines 255 – 256 of the original version). How is the comparison made of IOP elevation tolerance in this model versus whole eyes? This reviewer would expect a higher tolerance in whole eyes. Regardless, a citation is needed.
**RESPONSE.** In our model, the average IOP that disrupted the eye-glass slide seal was 117.3 ± 36.2 mmHg (Line 180), which is much higher than the highest IOP during cataract surgery for the bisected eye (55.8 ± 4.7mmHg) and the whole eye (55.3 ± 5.0mmHg) (Lines 196-197). Thus, this model can be used to mimic closed-eye surgery. As shown in Table 1, the highest IOP was not significantly different between the bisected porcine eye and the whole eye. (Table 1)

We have added the following sentences in our revised manuscript with a citation, as follows.”Khng et al. reported that the IOP was around 60-100 mmHg when the bottle height was at 130-150 cm during standard cataract phacoemulsification in cadaver eyes.” (Lines 238-240)

*Additional point 6*

Another limitation of this study is that the eyes are not kept at a physiologic temperature. This point should be noted along with the author’s view of its effects.

**RESPONSE.** Dipping the eye into liquid nitrogen for 5 seconds before bisecting the eye did not morphologically damage the ciliary body and zonular fibers. This was supported by our electronic microscopic study and thermographic analysis. This has been discussed in the revised manuscript, as follows. “However, our thermographic measurements showed that the temperature around the zonular fibers after dipping the eye into liquid nitrogen for 5 seconds was around 4º C, and scanning electron microscopy showed that the morphology of the PCSs was normal (data not shown).” (Lines 278-281)

**DISCRETIONARY REVISIONS**

*Additional point 7*

(Lines 171 – 174 of the original version). In the description of the 3 groups of eye sealing techniques, groups 2 and 3 are very similar, except that group 3 uses fresh eyes and allows 30 minutes of eye fixation versus 3. This point could be included to make this description more easily understood.

**RESPONSE.** Groups 2 and 3 are processed differently. We stated that Group 2 eyes were frozen for easy cutting and sealing was done for 3 minutes, while Group 3 eyes were not frozen before cutting and sealing took 30 minutes. Although eyes in Group 3 showed similar sealing strength, the difficulty in bisecting and longer sealing time are less favorable. This has been discussed in the revised manuscript.
Reviewer 2: Comments by reviewer Dr. Roland Ackermann

Comment 1
The manuscript needs to be spell checked, e.g:
l55: serviced -> served
l194: tolerated -> tolerate
l207: different -> difference

RESPONSE. This revised manuscript has been edited by a native English speaking Professor of Ophthalmology. In addition, the text has been spell- and grammar-checked.

Comment 2
The authors state that the IOP behaves similarly in bisected and whole eyes.
However, Fig. 3 shows arbitrarily chosen time frames without absolute time stamps.
The authors should provide information about the overall time dependence of the IOP for both cases in order that the reader may evaluate this similarity

RESPONSE. In the revised Figure 3, we have added a time scale for representative eyes from both groups. (Figure 3)

Comment 3
The use of the Tukey-Kramer’s test is an indication of unequal sample sizes, and indeed there are apparently ten points for group 1 and nine points for group 2 and 3 in Fig. 2 (though counting may be erroneous, as they are partially overlapping). However, according to l179, there should be ten samples for each group. The authors should comment on this discrepancy.

RESPONSE. Ten eyes each were tested in each group. As mentioned, some of the points for Groups 2 and 3 are overlapped. (Figure 2)

Reviewer 3: Comments by reviewer Dr. Peter Koulen

Comment 1
The manuscript needs to be extensively edited for grammar, syntax and spelling.

RESPONSE. This revised manuscript has been edited by a native English speaking Professor of Ophthalmology. In addition, the text has been spell- and grammar-checked.
Comment 2

Techniques and Methods would benefit from a standardisation of methods and materials, specifically with respect to group 3 and source and composition of wheat flour and glue.

RESPONSE. We have added more information regarding the weight of the glue and wheat flour applied for eye sealing (Line 111 and Line 115).

Comment 3

The authors need to identify quantifiable criteria used to make the new observation paradigm.

RESPONSE. The purpose of this study was to introduce a new method for viewing the PCSs during cataract surgery that mimicked human cataract surgery. The quantifiable data were obtained for evaluating the IOP at different steps of the surgery. Although quantification of the morphological changes of PCSs and IOP would have been helpful, these data were not given for the conciseness and clarity of this paper. Instead, we cited our previous publication regarding this issue (Lines 267-269).

Comment 4

The authors claim that they perform visualization in a 3-dimensional fashion, however, it remains unclear what makes the videography / recording 3-dimensional.

RESPONSE: We have presented data that supported our conclusion that the preparation of the eyes, momentary freezing, bisection, gluing, and operating conditions did not alter the morphology of the PCSs. We emphasize that this method allowed us to view and record the cataract surgery from the surgeon’s view and also record the movements and tensions in the posterior chamber, the camera’s view on the monitor during the surgery. To avoid confusing the readers, we have removed the term of 3-D from the revised manuscript.